DISSERTATION

ON

"CLINICAL AND NEUROPHYSIOLOGICAL STUDY OF NON-PARKINSONIAN TREMORS"

Submitted in partial fulfilment of

requirements for the degree of

D.M. NEUROLOGY (BRANCH – I)

of

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003.

AUGUST 2010

CERTIFICATE

This is to certify that this dissertation entitled **" CLINICAL AND NEUROPHYSIOLOGICAL STUDY OF NON-PARKINSONIAN TREMORS"** submitted by **Dr.R.CHANDIRA KUMAR** appearing for **D.M. Neurology** Degree (Branch - I) examination in **August 2010** is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

DEAN

Madras Medical College

Government General Hospital

Chennai – 600 003

Dr. R.M.Bhoopathy, M.D, D.M

Professor of Neurology

Institute of Neurology,

Madras Medical College

Government General Hospital

Chennai – 600 003

DECLARATION

I solemnly declare that the dissertation titled **" CLINICAL AND NEUROPHYSIOLOGICAL STUDY OF NON-PARKINSONIAN TREMOR"** is done by me at Institute of Neurology, Madras Medical College & Govt. General Hospital, Chennai, during **2008-2010** under the guidance and supervision of **Prof.R.M.Bhoopathy** ,

The dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of **D.M., Degree in Neurology.**

Place: Chennai

Date:

Dr. R.CHANDIRA KUMAR

Postgraduate Student
D.M. in Neurology,
Institute of Neurology,
Madras Medical College
Chennai-600 003.

ACKNOWLEDGEMENT

I gratefully acknowledge and sincerely thank the **DEAN, Dr.J.MOHANASUNDARAM**, ***M.D.*, *Ph.D.*, *D.N.B.*,** Madras Medical College, and Government General hospital, Chennai for allowing me to do this Dissertation and utilize the Institutional facilities.

I have great pleasure in expressing my sincere gratitude and respect to my **Prof. Dr.R.M.Bhoopathy, M.D.,D.M.,** Professor of Neurology, Institute of Neurology, Madras Medical College, Chennai, for his valuable suggestions, kind guidance, constant supervision and moral support for fulfilling this dissertation work.

This is one another fine moment to express my gratitude and indebtedness to my respected Professors **Prof. Geetha Lakshmipathy, Prof.A.V.Srinivasan and Prof. V.Natarajan** for their supervision and guidance in making this work successfully.

I profoundly thank my respected Professors, **Prof.C.Mutharasu, Prof.K.Bhanu and Prof. S.Gopinathan** for their advice, guidance, and valuable criticism which enabled me to do this work effectively.

I would like to thank our Assistant Professors **Dr.V.Kamaraj, Dr.S.Arunan, Dr.P.Muthukumar, Dr.D.Chezian, Dr.M.Jawahar, and Dr K.Kannan** for their cooperation and guidance.

I am thankful to all my postgraduate colleagues for their constant support and sharp constructive criticism.

I am thankful to the Neurochemistry laboratory, Barnard institute of Radiology, our EMG laboratory, and all technicians who helped me to conduct this study.

I should thank each & every patient who participated in this study for their whole hearted cooperation in making this study successfully.

****

INTRODUCTION

Tremor is a periodic movement about an axis, which distinguishes it from other movement disorders such as chorea, myoclonic jerks and tics which may not have a fixed period and may involve complex movements other than simple oscillation[1] .Tremors present commonly in neurology OPD.

Among these, majority of cases are Parkinsonian tremors, however non-parkinsonian tremors eg. Essential tremor, Exaggerated physiological tremor, drug induced tremor, rubral tremor, dystonic tremors etc are also seen. Essential tremors is one of the most common movement disorders.[2]

In population based studies, the prevalence of ET increases steadily with age, occurring up to in 10% of patients older than age 60 years with a median age of 15 years but there is a bimodal distribution.[2]

Tremors can be divided into two types – at rest and those seen on action. 'Rest' is only a relative term as some slight tonic postural maintenance is often required. Action tremors must be subdivided into those seen just with postural maintenance (postural or static tremor) and those requiring goal directed movements (intentional or kinetic tremor).

A third division of action tremor is those seen only with specific types of kinetic movements such as hand writing.[3]

Surface EMG (SEMG) is a technique to measure muscle activity noninvasively using surface electrodes placed on the skin overlying the muscle. Unlike needle EMG, SEMG electrodes record from a wide area of muscle territory, have a relatively narrow frequency band (range 20 to 500 Hz), have low signal resolution, and are susceptible to movement artifacts.[4] It can record both voluntary and involuntary muscle activity.

Of all the different types of movement disorders, tremors are probably the most common. These alternating, oscillating and rhythmical movements are perhaps the most simple and easily recognized abnormal movement, simple in the sense that it is the same pattern or movement over and over again. Yet for all the simplicity in the pattern of these alternating movements, their presence under certain conditions such as when the involved body parts is resting in repose or actively engaged in a motor activity adds a level of complexity to tremor, resulting in a classification based on what brings on the tremor. Thus differentiating the types of tremor makes the study of tremor much more complex than one might first think.[5]

Tremor Rating Scale (TRS) is a simple clinical rating scale for tremors which can be used in OPD and may be useful in monitoring patients response to treatment in numeric terms. This study is an attempt to classify and characterize non Parkinsonian tremors using clinical examination, TRS grading and surface EMG characteristics (synchronized, alternating or mixed burst patterns).

AIMS OF THE STUDY

1.To study the regional distribution of various etiological types of non-parkinsonian tremor disorders.

2. To investigate the diagnostic potential and the predictive value of routine tremor analysis with available neurophysiologic tests.

REVIEW OF LITERATURE

History of Tremors

Essential tremor is one of the most prevalent movement disorders and has affected people from the beginning of modern human existence. The distinct entity of essential tremor, however was not fully described until the end of the 19th century and the term 'essential tremor' was not routinely used by neurologist until the second half of the 20th century.[6] Documentation of tremor became somewhat more prevalent in India, from 5000 to 3000 BC.

The Ayurveda, which was the literature system of that time, makes many reference to tremors. The term *'kampa'* was used to indicate tremor and *'Kampavata'* meant imbalance due to tremor.[7] It was not until the times of Anno Domini that physicians became more illustrative when describing tremor.

Between 130-200 AD, Claudins Gaten of Pergamon, a Turkish physician who treated the gladiators was the first to describe tremors as an involuntary up and down motion. He wrote "no one trembles who does not choose to move his limb". This unquestionably equates his term "tremor" to what we routinely today call action tremor.[8]

During the 17th century, further distinction was made between action and rest tremor. In the year 1700, a Dutch physician named Gerhard Van Swetan differentiated between rest tremor and intention tremor. In 1817, the famous English general practitioner, James Parkinson, distinguished essential tremor from all other

tremors, including the resting tremor found in the disease that carries his names.[9] In 1888, the French neurologist Jean Martin Charcot concurred with this distinction.[10]

Neuropathology of Tremor

Essential tremor is the most common pathological tremor in humans and is estimated to be 10-20 times more common than Parkinson's disease. Essential tremor is regarded as a dysfunction within cerebral nervous system, but the site and nature of the pathological process remain unknown. Pathological studies of ET are scarce.

To date there are less than 50 essential tremor studies .The limited studies show that the pathology in essential tremor is in the cerebellum or its brain stem connections. Electrophysiological studies indicate that 58% of essential tremor cases have intention tremor resembling that seen in cerebellar disorder and some degree of hypermetria.

However most essential tremor patients do not manifest clinical ataxia or dysmetria. One well documented essential tremor patient had resolution of ipsilateral tremor following cerebrellar stroke.[11]

The MRI studies in this case indicated an ischemic lesion of the deep cerebellar nuclei and their efferent fibers into the superior cerebellar peduncle with involvement of the superior cerebellar cortex.

Interestingly alcohol ingestion, which decreases the amplitude of essential tremor in most patients has been noted to produce an increase of blood flow in the inferior olivary nucleus in essential tremor patients but not in control subjects.

Hassler in 1939 observed one patient of essential tremor with upper limb tremor and noted that the number of small neurons in the striatum was reduced.[12]

Mylbe and Van Bogaert did pathological studies in 2 patients and found neuronal loss in inferior olivary nucleus and cerebellar, dentate nucleus.[12] Rajput et al reported five pure essential tremor cases and found no histological abnormalities in brain.[14]

These studies indicate that pure essential tremor patients have no consistent brain pathology on routine histopathological examination.

Neurochemistry in Essential Tremor

In contrast to well defined biochemical defect in Parkinsonian's disease there are no characteristics findings in essential tremor. ET is a strictly human disorder. As yet there is no good animal model which could be used for biochemical studies of ET. Stibler and Kjellin reported abnormal CSF proteins in 94% of the essential tremor patients. Protein[14] Electrophoresis study in these cases was inconclusive.

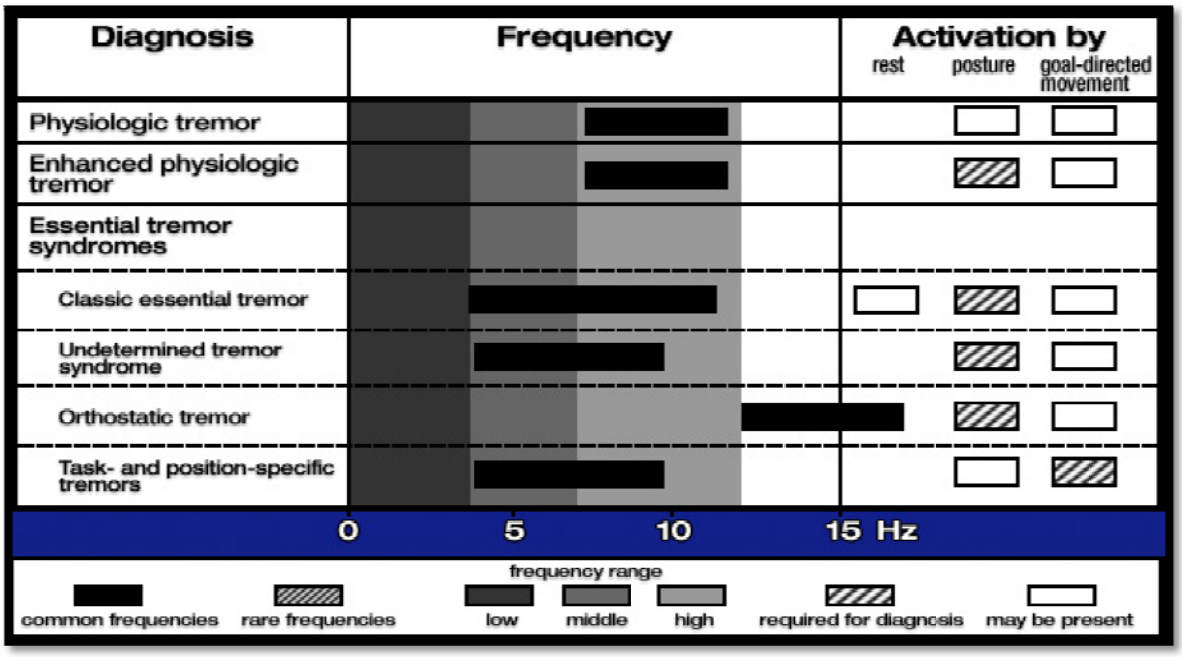
Mally and Baranyi in 1994 reported on CSF in 19 essential tremor cases a significant elevation in amino acid aspartate.[16] However a recent study reported no difference in ventricular CSF glutamate levels between essential tremor and Parkinson's disease.

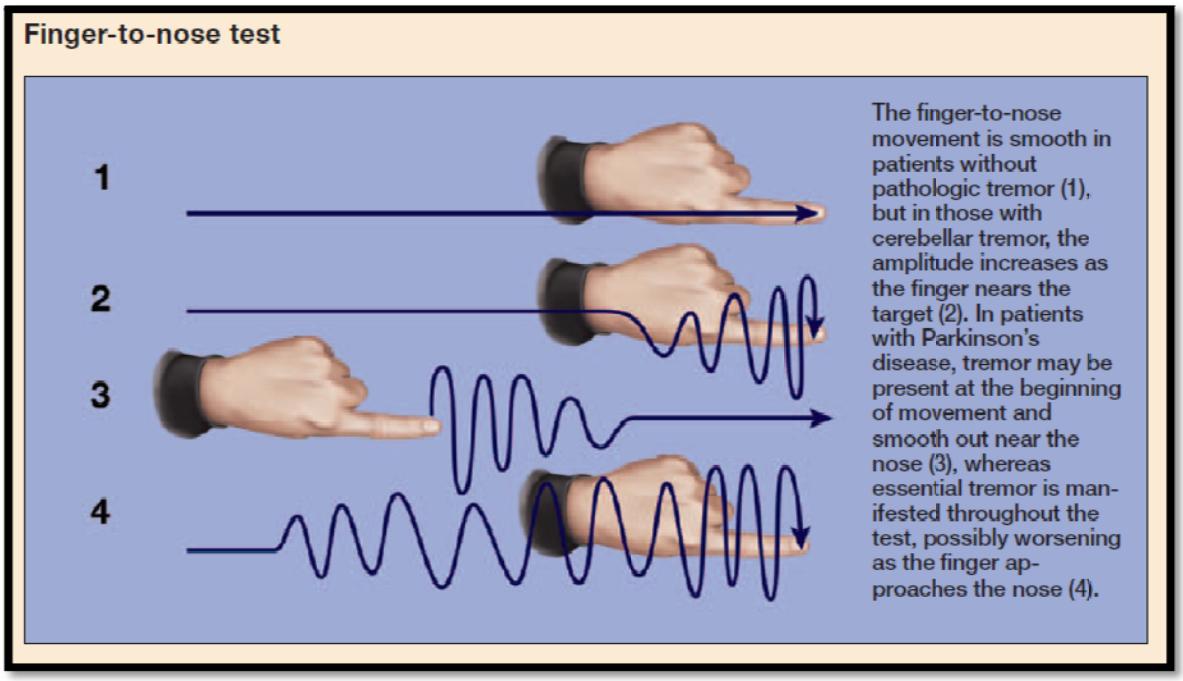
Adrenergic system modulation by beta-blockers is mandatory in essential tremor therapy. Selective beta-l antagonist are reported to be less beneficial than propranolol a non selective beta antagonist. The mechanism of action is believed to

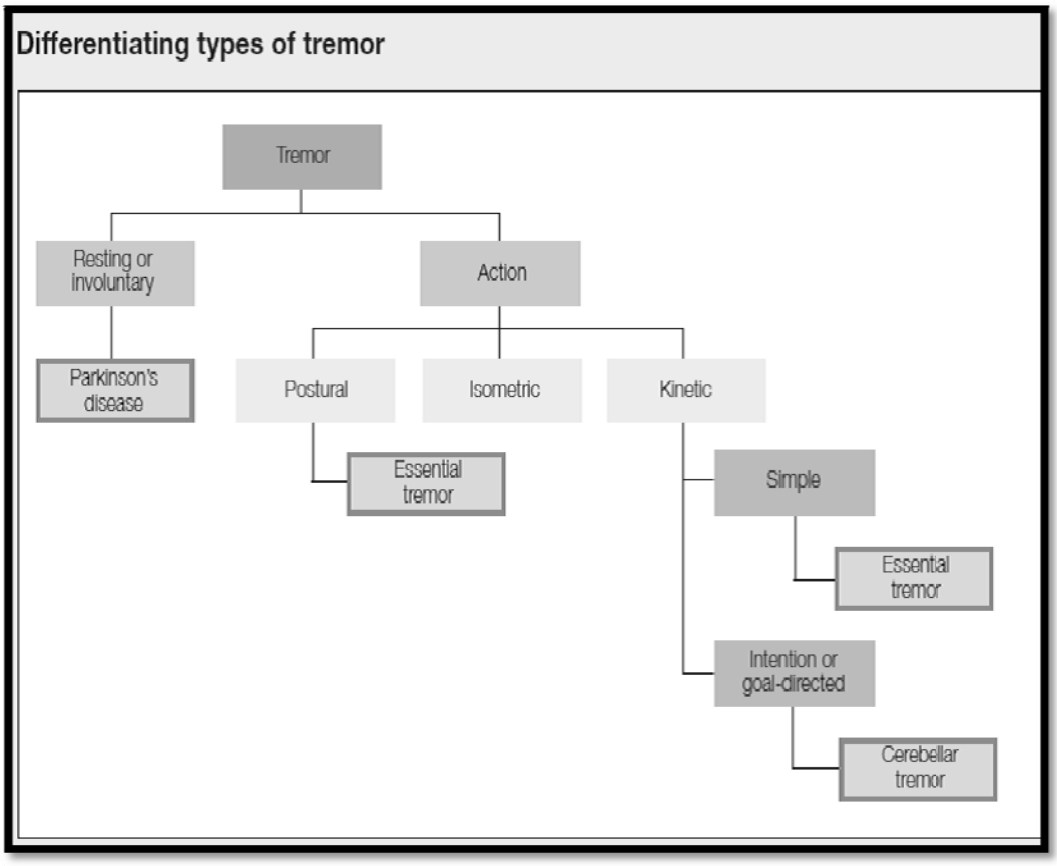
involve both peripheral and cerebral adrenergic effects of drugs. The peripheral effects are thought to be due to a blockade of beta 2 receptor in muscle spindle. Beta carboline alkoloids induce tremor when given to lab animals and to humans.

GABA is a inhibitory neurotransmitter which causes cellular hyperpolarization via its action on the chloride channel. Medications which potentiate GABA activity including barbiturate and benzodiazepine may be effective for essential tremors. Tang et al reported on the beneficial effects of baclofen a GABA , antagonist on harmoline induced tremors in rats. Gabapentin an anticonvulsant structurally similar to GABA has been reported as effective as monotherapy for essential tremor. But this has not been confirmed by others.[18]

Syndromic classification of tremor






Differentiating types of tremor
Tremor
Resting or involuntary
Action
Parkinson's disease
Postural
Isometric
Kinetic
Essential tremor
Simple
Essential tremor
Intention or goal-directed
Cerebellar tremor

Electrophysiological criteria for essential tremors

The sine guenon of essential tremor is a rhythmic 4-12 Hz of motor unit activity that forces the upper limbs into oscillation. Young patients exhibit higher tremor frequencies that often extend into the frequency range of physiologic hand tremor.[20]

Tremor frequency tends to decrease slowly at an average rate of 0.07 Hz per year. The frequency of oscillation is independent of reflex arc length and mechanical properties (inertia and stiffness of the body part).

Consequently the frequency of moderately severe (> 1cm) hand tremor changes less than 14Hz when large inertial diagnostic maneuver combined with EMG, Accelerometry and spectral analysis, has been used in the diagnosis of essential tremor and other action tremors of central origin. The diagnostic criteria proposed by movement disorder society are as follows,

Diagnostic criteria for essential Tremor

Diagnosis	Inclusion criteria	Exclusion criteria
Classic essential tremor	Either of the following is true: 1. Bilateral, largely symmetric postural or kinetic tremor of the hands and forearms that is visible and persistent. 2. Additional or isolated head tremor without evidence of dystonia (e.g., abnormal posturing)	1. Other abnormal neurologic signs, especially dystonia 2. Presence of known causes of enhanced physiologic tremor (e.g., drugs, anxiety, depression, hyperthyroidism), including current or recent exposure to tremorogenic drugs or the presence of a drug withdrawal state 3. Historic or clinical evidence of psychogenic tremor 4. Convincing evidence of sudden onset or stepwise progression (e.g., following a neurologic trauma) 5. Primary orthostatic tremor 6. Isolated voice tremor 7. Isolated position-specific or task-specific tremors, including occupational tremors and primary writing tremor 8. Isolated tongue or chin tremor 9. Isolated leg tremor
Indeterminate tremor syndrome	Satisfies the inclusion criteria for classic essential tremor, but the patient has equivocal neurologic signs or concomitant neurologic signs of doubtful significance (e.g., a mildly unsteady gait, mild dementia in an elderly patient, or mild extrapyramidal signs such as hypomimia, reduced arm swing, and mild bradykinesia)	Same as for classic essential tremor

Clinical and Surface EMG Tremor Analysis

Theoretically, tremor oscillations can emerge from two basic mechanisms. Any moveable limb can be regarded as a pendulum with the capability to swing rhythmically that is to oscillate. These oscillations will automatically assume the resonant frequency of this limb which is dependent on its mechanical properties, the greater its weight the lower its resonance frequency. As the limb mechanics and possibly reflex loops play a role in these oscillations they are termed 'mechanical-reflex-oscillation'.

The second basic mechanism of tremor is a transmission of oscillatory activity within the CNS to the peripheral muscles called 'central oscillation'. In contrast to the mechanical reflex oscillations, central oscillations occur at the centrally determined frequency and are independent of the limb mechanics. This crucial difference between the two basic mechanisms can be utilized to distinguish them. The limb mechanism can be influenced by putting additional weight on the limb under study.[21,22]

In 2004, Girowell, Alexendre, Kuliseusky, Jaime, Parchat Sedano, Berta, Barbanoj Manel studied 300 patients using electrophysiological surface EMG criterias found that these criteria showed a sensitivity (97.7%), specificity (82.3%), a positive predictive value of 95.1% and concluded that SEMG have high diagnostic and predictive value that justifies its practice in movements disorder clinics.[22]

Dr. Sybille Spicker et al, 1997, using a method of tremor quantification using longterm electromyography recording and measuring above method on UPDRS and

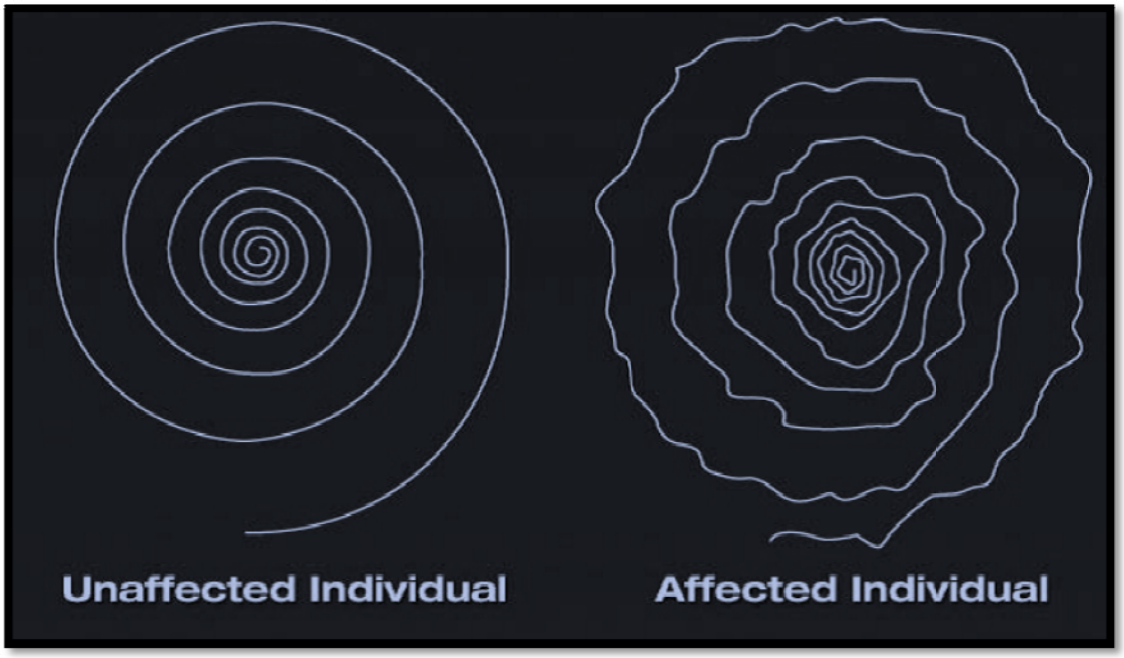
TRS (Tremor rating scale according to Bain et al) concluded that such studies are a valid and objective means of tremor quantification.[24]

In 1998, PE O' Suilleabhain and JY Matsumoto did time frequency analysis of tremors. They suggested coexistence of muscle groups physically contracting at consistently different instantaneous frequencies is evidence against a psychogenic activity of tremor.[25]

In 2000, J.L. Pullman, D.S. Goodin, AI Marquinez, S. Tabbal and M. Rubin published a special article regarding the clinical utility of surface EMG under the umbrella of American Academy of Neurology. They concluded based on class III data, SEMG to be considered an acceptable tool for kinesiologic analysis of movement disorders, for differentiating types of tremors, myoclonus and dystonia, for evaluating gait and posture disturbance and for evaluating psychophysical measures of reaction and movement time. (Type C recommendation)[3]

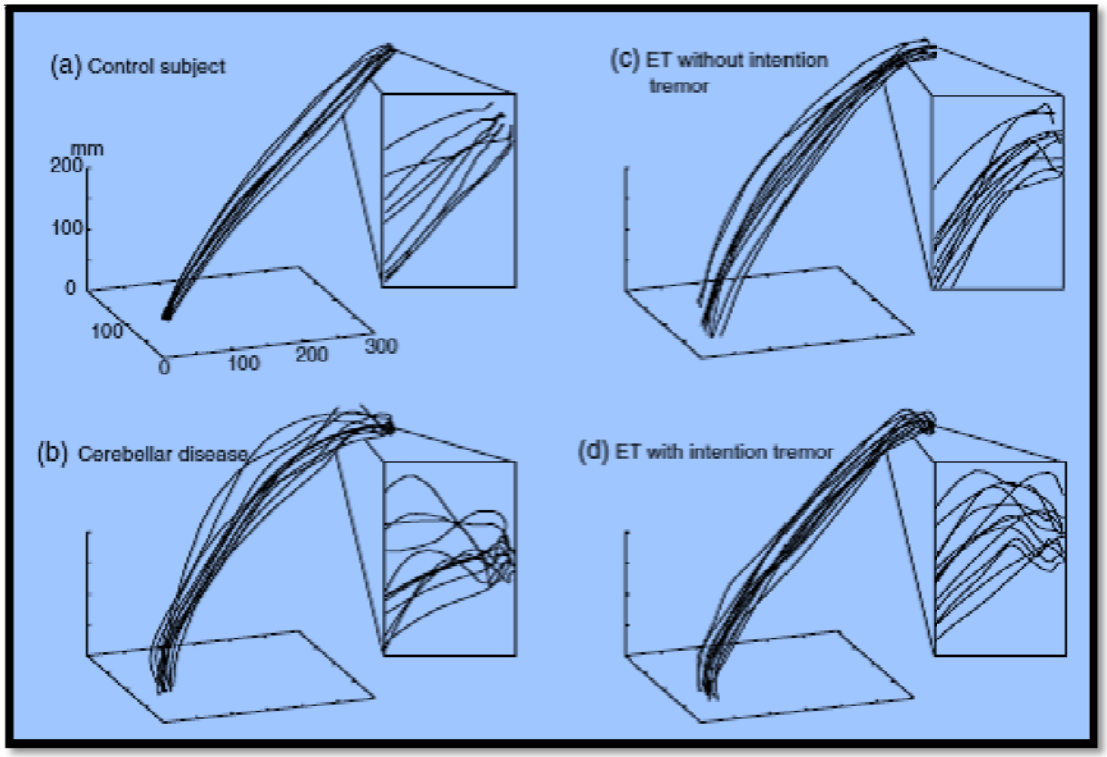
In, Indian studies, M. Mehindiratta, M. Satyawani, S. Gupta et al, studied in 2004, clinical and surface EMG characteristics of valproate induced tremors. Tremors typically were of high frequency (mean 10 Hz), low amplitude, short burst duration and burst pattern resembling benign essential tremors. [27]

The Clinical Assessment of Essential Tremor



An Archimedes spiral drawn by a normal person and patient suffering from essential tremor showing natural fluctuations in tremor magnitude.

Hand trajectories during a natural reach to grasp movement



Treatment of Essential Tremor

As a general rule, the more severe the tremor, the less likely the chance that oral medications alone will provide sufficient long-term control of tremor [35].

It was Marshall, 1968, who suggested beta-adrenergic blockers in essential tremors. While several beta-blockers, including sotalol and metoprolol, appear to be effective in the management of ET, propranolol, a nonselective antagonist, has been the most consistently studied and is more effective than relatively selective beta1-antagonists (Pourfar and Louis, 2006).

The efficacy of propranolol appears to be mediated mainly by peripheral and possibly central mechanisms of action. Propranolol can be given as a standard or long-acting formulation. Initial dosing with the standard formulation begins with 10 mg/d to 20 mg/d. This is then titrated each week, as tolerated, to as high as 320 mg/d, with an average being 120 mg/d[35].

Approximately 45% to 75% of patients report a reduction in arm tremor from propranolol as compared with placebo. The response is less satisfactory in the treatment of voice and head tremor. Side effects, although generally mild to moderate, occur in over half of patients.Fatigue, depression, orthostatic changes in blood pressure, impotence, and exercise intolerance are among the more common side effects. Evidence of the efficacy was confirmed by Winkler and Young.[28]

In 1982, Findley and Calzetti reported primidone to be effective in treating essential tremor.[29] The parent compound, primidone, is partially metabolized to Phenobarbital and 2-ethyl-2-phenylmalonamide, of which the former has some therapeutic efficacy as well. Primidone and propranolol have been compared directly in several clinical trials, which suggest their efficacy is similar, although some evidence demonstrates that primidone is better tolerated in the long-term management of ET.

A drawback of primidone, however, is a relatively common acute adverse reaction composed of nausea, vomiting, or ataxia, which can occur in more than 20% of patients who are starting the drug; this usually requires the discontinuation of the drug. The usual starting dose of primidone is 25 mg at bedtime. This is increased by 25 mg/wk in three divided doses up to 100 mg/d and then increased by 50-mg increments up to 1000mg/d with an average dose being 750 mg/d.

Studies have demonstrated a 60% to 75% improvement in tremor amplitude compared with placebo. In 1986, Koller and Royse reported that primdone was 40-50% efficacious in treating ET.[31]Like propranolol primidone is often less effective in the management of voice and head tremor than in limb tremor. The combination of these two has proven to be of benefit in some cases (Pourfar and Louis, 2006).

In patients who do not benefit from either of these two medications or whose response is suboptimal, add-on or alternative pharmacotherapy is a reasonable next step.

Gabapentin was superior to placebo in two of three trials. It is usually titrated from a starting dose of 300 mg/d to up to 1800 mg to 2400 mgs.

Alprazolam (0.75 mg/d to 2.75 mg/d) also has shown to be of benefit but is frequently limited by sedation.

In 2002, Conoor found topiramate to improve functional measures of essential tremor.[30] Topiramate (25 mg/d to 400 mg/d) has recently been the subject of study and has demonstrated modest to moderate efficacy in ET.

In addition, 1- octanol (Bushara et al, 2004), sodium oxybate (Frucht et al, 2005), and levetiracetam (Bushara et al, 2005) have shown some promise in the treatment of ET, and further trials are warranted.

Botulinum toxin injections are another modality known to be useful for treating essential tremors. In 1998, Modugero et al studied the effect of botulinium toxin type A injection in 10 patients with 1 essential tremors and hypothecated that it could be used effectively in ET.[32]

In, 1996 Jankovic et al conducted a randomzed, double blind, placebo controlled trial of botulinum toxin type A in essential tremor which showed a significant improvement of postural hand tremor, but not kinetic tremor. However it has been more successful in treating head and voice tremor.[33] Voice tremor is frequently reduced with 0.6 U to 15.0 U injections to the vocal cords.

In 2003, Rehncrona et al studied the efficacy of deep brain stimulation (DBS) after electrode implantations in the ventralis intermedius nucleus of thalamus in 39 patients with severe tremor. They conclude that thalamic stimulation can efficiently suppress severe tremor in essential tremor and parkinson's disease > 6 years after implantation. Thalamic stimulation is commonly used today and is preferred over surgical lesions.[34]

Dystonic tremor syndromes occur in patients with dystonia and tremor in the same body part affected by dystonia (dystonic tremor; e.g., tremulous writer's cramp), or in a body part not affected by dystonia (tremor associated with dystonia; e.g., postural tremor of the arms indistinguishable from ET in a patient with cervical dystonia).

Dystonic tremor occurs in approximately 70% of patients with cervical dystonia. A diagnosis of dystonic head tremor is supported by an irregular, jerky, and often complex tremor pattern, abnormal posturing (although this may only be apparent during complete relaxation, distraction, or walking), a tremor amplitude that

varies depending on head position, and use of a sensory trick to reduce tremor amplitude.

Botulinum toxin has been shown to be effective in dystonic head tremor , but in clinical practice abnormal head and neck postures appear to be more responsive to this treatment than does tremor with an average optimal dose of 200 U injected into the sternocleidomastoid, splenius, or trapezius muscles, depending on the individual patient's situation.Anticholinergics and clonazepam are occasionally effective.[40]

Task- and Position-specific Tremors

Primary writing tremor is perhaps the most common example and has been subdivided into tremor occurring only during writing (task-specific writing tremor) and tremor occurring when the hand adopts a writing position (position-specific writing tremor)

Isolated voice tremor is another task-specific tremor that is thought to occur either as a variant of laryngeal dystonia or ET. This tremor may be difficult to distinguish from ET or early PD, and the distinction between this condition and dystonic writing tremor or writers' cramp with coexisting tremor is uncertain. Pharmacotherapy is often disappointing, although propranolol, primidone, and alcohol can be tried and botulinum toxin may have an effect .

Training the patients to write with the other hand occasionally helps. Isolated voice tremor is another task-specific tremor that is thought to occur either as a variant of laryngeal dystonia or ET. Dystonic voice tremor is thought to be more likely if tremor ceases varies with changes in pitch or with singing or emotional speech production. Other task specific tremors occur uncommonly and include those associated with sporting endeavors or with playing musical instruments.

Enhanced Physiologic Tremor

Enhanced physiologic tremor describes a tremor that is easily visible, is usually postural, and has a frequency of typically 8–12 Hz in the outstretched hands and quantitative computerized tremor analysis can be helpful; unlike ET, in patients with enhanced physiological tremor, the addition of an inertial load (weight) on the tremulous outstretched arm will result in a reduction in tremor frequency.

It usually occurs in association with anxiety, stress, muscular exertion, hypothermia, hypoglycaemia, pheochromocytoma, thyrotoxicosis, alcohol withdrawal, or drugs (e.g.beta receptor agonists, sodium valproate,lithium, neuroleptics, and tricyclic antidepressants). Management should be directed toward removing precipitating causes, although propranolol in small doses can be effective

Cerebellar and Holmes' Tremor

Pure or dominant intention tremor that may be irregular in frequency (generally less than 5 Hz) and amplitude can be regarded as cerebellar tremor.

Tremors including slow postural tremors of the head and trunk (titubation) or proximal muscle groups that are often marked during stance can also occur in association with cerebellar dysfunction In view of the variety of locations of lesions that can cause this tremor (including pons, thalamus and subthalamus in addition to the midbrain) because of the early description of this syndrome by Gordon Holmes .

The rest component that best distinguishes this tremor from cerebellar tremor is probably explained by frequent pathologic involvement of the nigrostriatal system (which is also affected in PD) and interruption of a combination of pathways traversing the midbrain. The etiology is most commonly vascular or head trauma, although infection, multiple sclerosis, tumors, and radiotherapy .

Few data are available to support the use of specific medications, and the treatment of cerebellar tremor remains difficult (Fox et al, 2004; Koller 1984; Seeberger and Hauser 2005). Carbamazepine (400 mg/d to 600 mg/d) has been shown in two studies to lower the amplitude of cerebellar tremor (Sechi et al, 1989), and isoniazid (1000 mg/d to 1200 mg/d) has been effective in some but not other trials (Hallett et al, 1985; Seeberger and Hauser, 2005).

Other agents that have been effective in some patients in small trials include topiramate (50 mg/d to 200 mg/d) (Sechi et al, 2003) and buspirone (60 mg/d) (Trouillas et al, 1997). Both thalamic DBS surgery and thalamotomy play a role in the surgical treatment of severe cerebellar tremors (Bittar et al, 2005; Seeberger and Hauser, 2005).

Peripheral Neuropathy Related Tremor

Action tremor resembling ET may occur in the setting of peripheral neuropathy of a variety of causes (eg, diabetic, uremic, alcoholic, compression, motor neuron disease, or familial) (Said et al, 1982) but demyelinating neuropathies, and especially dysgammaglobulinemic neuropathies, are frequent causes of such tremor.

The tremors are mostly postural and kinetic tremors. The frequency in hand muscles can be lower than in proximal arm muscles in patients with gammopathies. It should be mentioned that abnormal position sense is not a required condition for the diagnosis. The pathophysiology of this tremor is thought to result from the abnormal interaction of peripheral and central factors. On tremor analysis, inertial loading leads to a decrease in tremor frequency, indicating a tremor with a peripheral generator A low dose (10 mg/d to 40 mg/d) of a beta adrenergic blocking agent may be beneficial. Thalamic DBS is not a recommended treatment because the tremor is peripherally rather than centrally generated.

Psychogenic Tremor

Psychogenic tremor occurs in the setting of a variety of psychiatric disorders By history, the tremor typically has a sudden onset with maximal tremor at commencement rather than being an insidious, slowly progressive disorder.

On examination, the tremor may be characterized by non-physiological or unusual features (eg, tremor exhibits variable frequency or direction, or an unusual combination of rest, postural, and kinetic tremors is present) as well as by the presence of entrainment (a change in the frequency of the limb tremor to match the frequency of a repetitive movement that the patient is performing with the contralateral limb), distractibility (ability to lessen the tremor by diverting the patient's attention from the tremor), and suggestibility (the ability to trigger or relieve the tremor with unusual interventions).

The initial step in the treatment of psychogenic tremor is establishing the neurological diagnosis. The next step, through psychiatric consultation, is to establish an underlying psychiatric diagnosis. The use of a neurobiological explanation for the patient's symptoms is recommended. The long-term treatment can only be successful in patients who are willing to accept the diagnosis and work closely with a psychiatrist.

Palatal tremor syndrome

Palatal tremor can be separated into two forms.

Symptomatic palatal tremor is characterized by:

1. Preceding brain stem cerebellum lesion with subsequent olivary hypertrophy, which can be demonstrated with magnetic resonance imaging (MRI)scans.
2. Rhythmic movements of the soft palate (levator veli palatini) and often other brain stem-innervated or extremity muscles.

Essential palatal tremor' is characterized by:

1. Absent preceding lesions and absent olivary pseudohypertrophy.
2. The patient usually has an ear click. The rhythmic movements of the soft palate mainly involve the tensor veli palatini. Extremity or eye muscles are not involved.

Primary orthostatic tremor

Orthostatic tremor is a unique tremor syndrome characterized by:

1. A subjective feeling of unsteadiness during stance but only in severe cases during gait; patients rarely fall. None of the patients have problems when sitting and lying.
2. Sparse clinical findings that are mostly limited to a visible and occasionally, only palpable fine amplitude rippling of the leg (quadriceps or gastrocnemius) muscles when standing.
3. The diagnosis that can be confirmed only by EMG recordings (for example, from the quadriceps muscle) with a typical 13-18-Hz pattern.

All of the leg, trunk, and even arm muscles can show this tremor, which is typically absent during tonic activation while the patient is sitting and lying.

The diagnosis critically depends on electromyographic (EMG) confirmation of the high-frequency EMG pattern because other tremors or symptoms (for example, akathisia, cerebellar stance tremor) during stance can occur with similar complaints.

Hereditary Geniospasm

Hereditary geniospasm, or trembling chin, is an unusual condition with autosomal dominant inheritance with linkage demonstrated to chromosome 9q in one of two British families . The involuntary episodic tremor of the chin and the lower lip has a frequency of approximately 8–10 Hz and there is an association with otosclerosis and deafness in some cases. Episodes typically start in early childhood, may improve in adulthood and can be precipitated by stress, concentration, and emotion. Botulinum toxin injection into the mentalis muscle is sometimes helpful.

MATERIALS AND METHODS

Place of study	:	Institute of Neurology, Government General Hospital, Madras Medical College, Chennai -3.
Type of study	:	Prospective, Clinical and Investigatory Study
Duration of study	:	2 years (January 2008 to January 2010).
Ethical committee	:	Present dissertation was approved by the Institutional Ethics Committee.
Consent	:	Informed written consent was obtained from all the participants.

Case selection

Patients with clinical symptoms suggestive of tremulousness were selected from the Neurology OPD and movement disorder clinic, Institute of Neurology, Madras Medical College, Chennai-3.

A. Inclusion criteria

1. Patients who presented with non-parkinsonian tremors.Patients under treatment (eg. With beta-blockade) whose drugs were stopped for 48 hours prior to study.
2. Patients who are conscious and cooperative for the electrophysiological study.
3. Patients who do not have orthopedic problems like fracture, joint arthritis.
4. A prolonged duration of tremor (more than five years).

B. Exclusion criteria:

1. Patients with parkinsonian tremors.
2. Patients having complex movement disorder apart from tremor.
3. Patient who are uncooperative for surface EMG.
4. Patients who are in altered behavior or sensorium secondary to a metabolic or systemic problems and those less than 12 years in age.

Materials:

The total number of 88 patients who satisfied the inclusion criteria formed the final materials of the present study.

Methods:

All subjects gave their informed consent prior to the study followed by

Step 1

Each patient underwent detailed history regarding age of onset of tremor, the duration of tremor, course of disease, activities inducing and aggravating it as well as relieving factors, family history, symmetry, drug history, substance abuse which was done according to the screening questionnaire for ET proposed by Louis et al as given below.

Screening Questionnaire For Essential Tremor

Twelve screening questions for ET:

1. Do you often have shaking or tremor that you can't control?
2. Do other people often tell you that you have a tremor?
3. Has a doctor diagnosed you as having familial tremor or benign essential tremor?
4. Do you often have shaking or tremor in your hands or arms that you can't control?
5. Does your head often shake uncontrollably?
6. Do you often have an uncontrollable tremor anywhere else in your body (legs, voice, mouth, chin, chest, other)?
7. Does your voice almost always tremble when you talk?
8. Does your hand usually tremble when you hold a pen or write your name?
9. Do you have a problem because your hand shakes when you drink or pour from a cup or a glass?
10. Do you have a problem because your hand shakes when you hold a fork, spoon, or knife?

11. Does shaking or tremor make you spill when drinking from a cup or eating soup with a spoon?

12. Do your hands tremble uncontrollably when you button your shirt?

Step 2

Tremors were clinically grouped on the basis of Tremor Investigation Group (TRIG) classification and Tremor Rating was done on the basis of The Tremor Rating Scale (TRS) provided by the members of the Tremor Research Group (TRG) and consists of items assessing action tremor in the head, voice, limbs and trunk. It requires tests of pouring water between two cups, drinking water from a cup, using a spoon to drink water, finger nose movements and drawing Archimedes spirals with hands. All patients were rated by examiner and simultaneously videotaped.

NIH Collaborative Genetic Criteria Tremor Severity Scale

Grade 0	=	None
Grade 1	=	Slight; barely perceivable; may be intermittent
Grade 2	=	Moderate; amplitude <2 cm excursion; may be intermittent
Grade 3	=	Marked; amplitude 2–4 cm excursion
Grade 4	=	Severe; amplitude >4 cm excursion.

This tremor rating scale is given in annexure-2

At least 3 months apart after the initiation of treatment, patient was reexamined with TRS for assessing test-retest reliability and concordance between live and videotaped assessments.

Step 3

All the patients underwent surface EMG recordings, in each position, on the limb most involved. The electromyographic (EMG) activity accompanying tremor may be recorded by pairs of disc electrodes arranged over the muscles involved in generating tremor and The mean tremor frequency (Hz), amplitude (mV), burst duration (m/sec), the tremor pattern (synchronous or alternating) and the 'mode locking' of the phases of the EMG bursts in agonist and antagonist pairs of muscles in various maneuvers like finger to nose in a horizontal plane with the arms abducted horizontally, elbows directed laterally and the wrists and index fingers straight.

Blood Investigation-Thyroid profile, blood sugar, renal function test, peripheral smear, rheumatologic workup and Neuroimaging (CT brain and MRI brain) for appropriate patients

Step 4

ET patients were further classified clinically by,

Definite ET - family member with history of tremor personally examined

Probable ET - if at least five questions answered as 'yes' from the screening questionnaire

Possible ET - if at least three questions were answered as ‘yes ‘from the screening questionnaire

The results were compared with the criteria laid down by the MDS Consensus Statement for concordance. The findings were entered in the proforma. (Copy of proforma enclosed)

RESULTS AND ANALYSIS

A total of 88 patients aged above 12 years who came to Neurology OPD and movement disorder clinic, Government General Hospital, Chennai between January 2008 to January 2010 with clinical symptoms suggestive of tremulousness and who satisfied the inclusion and exclusion criteria were included in this study.

Total number of patients - 88

- Male patients - 52 (59.00%)
- Female patients - 36 (40.9%)
- Male: Female ratio - 1.45:1

AGE DISTRIBUTION:

- The maximum numbers of patients were in the age group between 50 and 59 years, followed by the age group between 40 and 49 and 30 and 39 years. Table 1 shows the age distribution in this study

Table 1 : Age Distribution

Age group in years	***No. of Patients***	***% of Total Patients* (88)**
13-19	5	5.68
20-29	11	12.5
30-39	14	14.77
40-49	20	17.0
50-59	23	22.72
60-69	9	4.54
70-79	6	4.54
Total	88	100

Table 2: Age Distribution (n=88)

N	**88**
Mean	42.63
Median	30.00
Mode	22.00
STD. Deviation	19.53
Minimum	14.00
Maximum	76.00

Mean age of studied cases is 42.63 years.

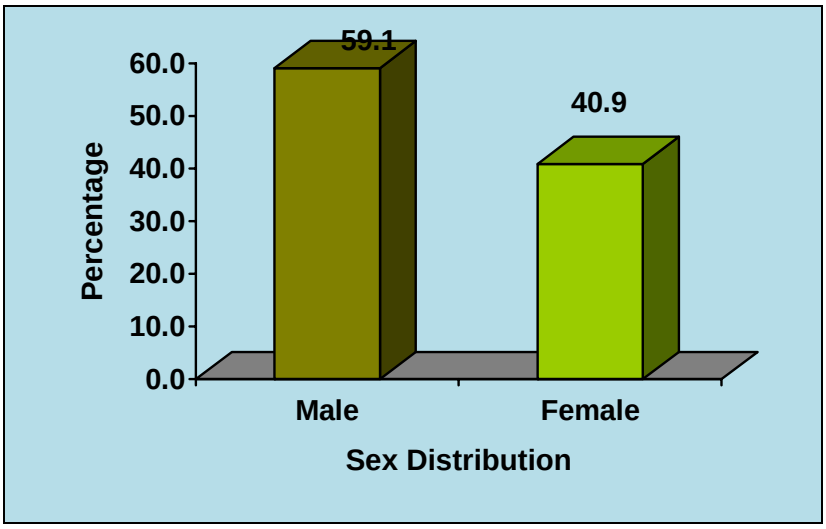
SEX DISTRIBUTION:

- There were 52 males (59.1%) and 36 females (49.9%) among the 88 patients in this study.

TABLE 3: SEX DISTRIBUTION IN THIS STUDY

Sex	***No. of Patients***	***% of Total Patients (88)***
Males	52	59.1
Females	36	49.9
Total	***88***	***100***

Figure 1: Sex Distribution



AGE AND SEX DISTRIBUTION:

- The predominant age group in both Male and female was between 40 and 49 years.
- Around half of males (49.9%) were in the age group between 40 and 59 years and half of females (47.2%) were in the age group between 40 and 59 years.

Table 4: Age Distribution Based On Sex

Age group in years	***Males (%)***	***Females (%)***
13-19	1(3.1)	4(11.1)
20-29	8(15.3)	3(8.33)
30-39	8(15.3)	6(16.6)
40-49	12(23.0)	8(22.2)
50-59	14(26.9)	9(25.0)
60-69	5(9.6)	4(11.1)
70-79	4(7.69)	2(5.55)
Total	**52*(100)***	**36*(100)***

Table 5: Type of Tremors (n=88)

Type	No. of Patients	Percentage
Essential Tremor	52	59.1
Dystonic Tremor	8	9.1
Task Specific Tremor	6	6.8
Drug Induced	6	6.8
Psychogenic tremor	4	4.5
Physiological Tremor	3	3.4
Cerebellar/rubral Tremor	3	3.4
Thyrotoxic tremor	3	3.4
Neuropathic tremor	3	3.4
Total	88	100

Essential Tremor (ET) was the most common non Parkinsonian tremor 59.1% (n=52).

Essential Tremor patients

A total of 52 patients (38males, 14 females) of ET were seen with mean age of 45.8 ± 16.0 years (range: 14 to 76 years). Progression of symptoms was reported in 25 (48.07%), while the rest felt that the disorder was static. Thirty seven patients had symmetrical involvement of both sides, the rest observed one of the sides to be worse affected. However, the difference observed in most patients was only mild.

No patients had dystonia of any body part. Bilateral hand tremor, either isolated or with involvement of other body parts was seen in 46 (88.46%), head tremor in 15 patients, lower limb tremors in 8 patients, while voice tremor was

observed in only 6 patients. Rest tremor was observed in 6 (11.53%) patients, though all patients had either or both of postural and kinetic tremor. High frequency tremor was seen in all the patients.

Alcohol responsiveness could be tested only in 9 patients, as the rest were teetotalers. Only three of these patients reported improvement with alcohol.

All patients reported disappearance of the tremor with rest, and aggravation with emotional stress.

Positive family history was found in 24 out of the 52 (46.5%) patients of ET, it was definite in 4, probable in 15 and possible in 6 patients. Three patients reported family history of Parkinson's disease; also. An autosomal dominant pattern was observed in 8 patients (36.4%), while in the rest, no conclusive inheritance pattern was observed.

Table 6: Clinical characteristics of patients with essential tremor [n=52]

Clinical feature	Number of patients	Percentage
Distribution:		
Hand	46	88.46
Head	15	28.84
Voice	6	11.53
Lower limb	8	15.38
Progressive disease	24	46.15
Symmetrical involvement	34	65.38
Rest tremor	6	11.53
Alcohol responsiveness	3	5.76
High frequency (8-12 Hz)	52	100

DURATION OF SYMPTOMS IN ET PATIENTS

- Most of the males (42.1) and females (42.8) had symptom duration of 2 -3 years

Table 7 : Duration Of Symptoms

Duration	Males (%)	Females (%)	Total (%)
< 2years	6(15.7)	2(14.2)	8(15.3)
2 years – 3 years	16(42.1)	6(42.8)	22(42.3)
2 years-5 years	12(31.5)	4(28.5)	16(30.7)
5 years and above	4(10.5)	2(14.2)	6(11.53)
Total	38(100)	14(100)	52(100)

DURATION OF SYMPTOMS WITH TREMOR SEVERITY IN ET PATIENTS

- Most of the patients with more than 5 years of symptoms had severe degree of tremor (10.5%). Those patients with duration less than 2 years had mild degree of tremor (15.7%).
- As the duration increases, there was a progression from mild to severe degree of tremor.

In this study, 6 in 52 patients with ET had rest tremor. The progression of the disease was slow in these ET patients, who reported tremor exacerbation after a mean of 4.2 years and involvement of a new anatomical region after a mean of 5.4 years. The tremor was associated with disease that was more severe, more disseminated (extending to other regions), and of longer duration. The basis for the rest tremor could be basal ganglia involvement, raising the possibility that the pathologic process responsible for ET may extend to these structures [42].

Table 8: TRS and Frequency Ranges

Type	TRS	Frequency
Essential Tremor	7-19.5	6-16
Dystonic Tremor	8-9	7-8
Task Specific Tremor	5-8	13-16
Drug Induced	11-24	6-12
Psychogenic tremor	Variable	Variable
Physiological Tremor	3.5	3.5
Cerebellar/rubral Tremor	5-23	5-8
Physiological tremor	3.5-4.5	10-12
Neuropathic tremor	5-6	10-12

Table 9: TRS Score and Frequency Analysis

		Number of Patients	Mean	Std. Deviation
TRS	ET	52	11.46	3.21
	Others	36	10.39	7.70
	Total	88	11.02	5.36
Frequency	ET	52	9.69	3.06
	Others	36	10.88	4.04
	Total	88	10.18	3.45

The mean TRS score in essential tremors is 11.46 ± 3.21 and mean frequency 9.69 ± 3.06 Hz.

Table 10: TRS and Frequency Ranges

	Tremor type	Minimum	Maximum
TRS	ET	7	19.5
	Others	3.5	24
	Total	3.5	24
Frequency	ET	6	16
	Others	6	16
	Total	6	16

The TRS range observed in study was 3.5 – 24 and frequency range 6 - 16. Essential Tremors showed TRS range from 7-19.5, frequency 6-16 Hz.

Table 11: Synchronised Surface EMG Pattern (n=88)

	No. of Patients	Percent
Yes	48	54.5
No	40	45.5

About 54.5% of patients showed synchronized Surface EMG pattern.

Figure 2 : Synchronized surface EMG pattern (n=88)

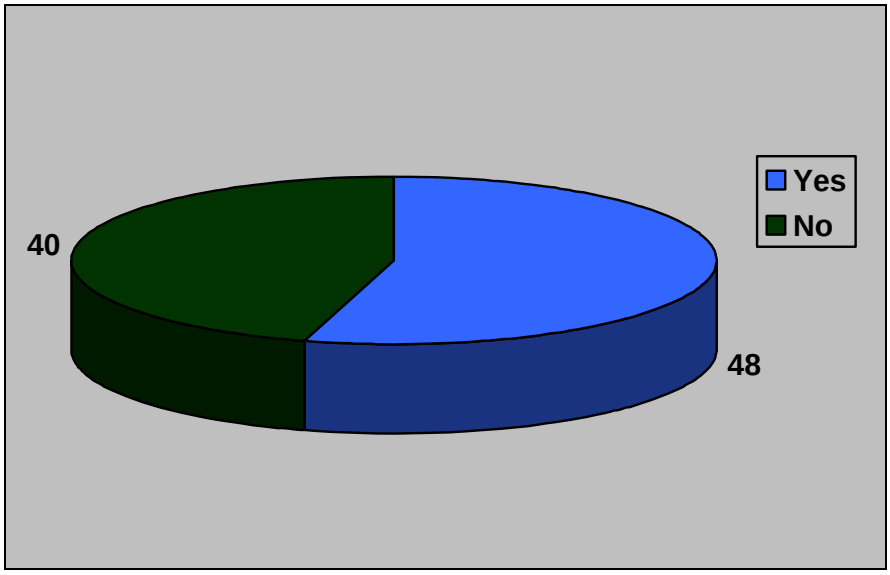


Table 12 : Synchronized EMG Pattern in Essential Tremor (n=88)

Type of Tremors	Synchronised		
ET	Yes	No	Total
Number of Patients	40	12	52
% within ET	76.9%	23.1%	100%
% within Synchronised	83.3%	30.0%	
Others			
Number of patients	8	28	36
% within others	22.2%	77.8%	100%
% within synchronized	16.7%	70.0%	
Total	48	40	88
% with types	54.5%	45.5%	100%

About 76.9% essential tremors showed clinical synchronized EMG burst pattern p-0.011 which is statistically significant ($p < 0.05$). Also ET was the commonest tremor among all tremors showing synchronized pattern (83.3%).

Figure 3 : Essential Tremor Showing Synchronization (n=52)

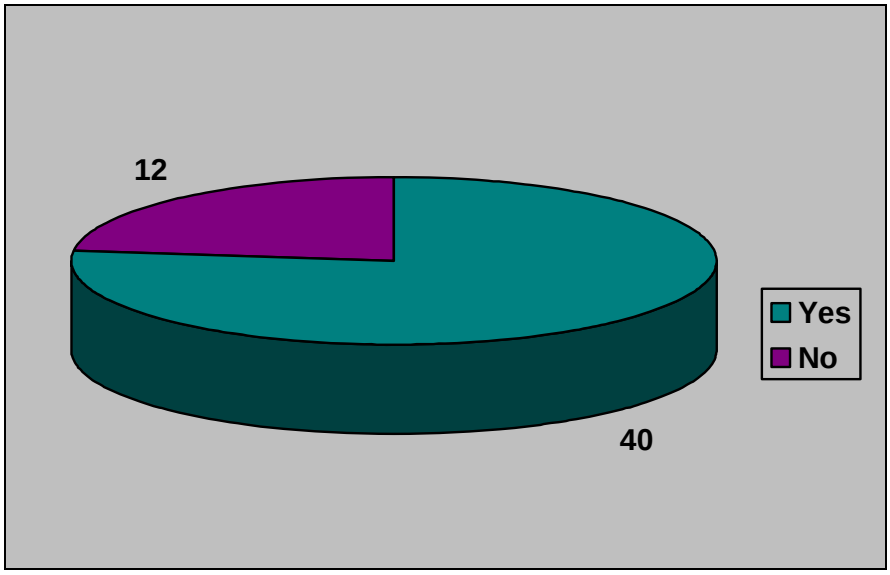


Table 13 : EMG patterns in essential Tremor (n=52)

Total	Synchronised + Mixed	Only Synchronised	Only Mixed
40	12 (23.07%)	28(53.84%)	12

About 53.84% essential tremor patients presented with only classical synchronized pattern. 23.07% of essential tremor patients had synchronized mixed pattern. None of the 52 essential tremor patients showed alternating tremorogram.

Figure 4 : **EMG patterns in ET (n=52)**

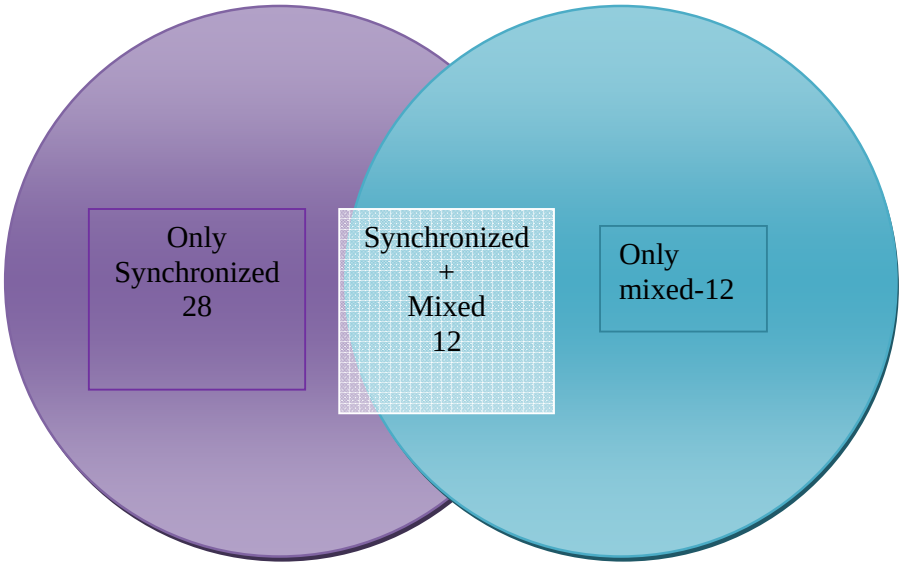


Table 14 : High Frequency EMG in the total patients (> 10 Hz) (n=88)

	No. of Patients	Percent
Yes	36	40.9
No	52	59.1

About 40.9% patients presented with high frequency tremors confirmed on surface EMG i,e. > 10 Hz.

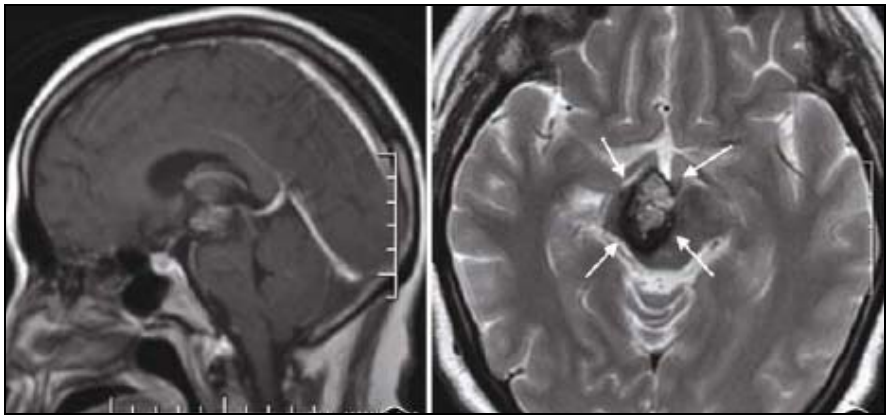
Dystonic Tremor patients

All 8 patients with dystonic tremor had asymmetric, multiplanar tremor, with changing frequency and amplitude in different postures. All patients had bilateral hand tremor, while 3 among these 8, had associated writer's cramp. No patients had dystonia of other body parts.

Neuroimaging was abnormal in three patients (one cerebellar infarct, one midbrain tumour and one post head injury-cerebellar atrophy)

42-year-old woman showed combination of rest and postural and kinetic tremors with a lower frequency varying from 2 to 5 Hz, higher during active movement and disappear during sleep.The amplitude at rest was small, but on attempting posture it become uncontrollable. In addition she had right partial 3rd nerve palsy and left hemiparesis with MRI brain showing a lesion suggestive of cavernoma that is shown in figure 5.

Figure-5



Thyroid function test was abnormal (hyper function) in three patients with enhanced physiological tremor and responded partially with propronolol and antithyroid drugs.

Nerve conduction study was done in three patients (one HMSN, One AMSAN, one CIDP), showed the features of motor, sensory axonal neuropathy.

DISCUSSION

Tremors are among common movement disorder observed in clinical practice. Clinical types of non-parkinsonian tremors were studied along with surface EMG and a clinical scoring system.

In our study, as previously described, the age range was wide, but males were thrice as frequent as females. The reasons for male preponderance in India are several; women in India usually ignore symptoms, especially those which do not hamper daily activities. Long-standing tremor with positive family history is easily diagnosed by general physicians.

Essential tremor is one of the most common movement disorder in clinical practice as stated by Joseph Jankovic and K.M. Shannon.[1] In our study 59.1% cases among the studied non-parkinsonian tremors were essential tremors. It was followed by Dystonic Tremor(9.1%) and Task Specific Tremor (6.8%), Drug Induced(6.8%), Psychogenic tremor (4.5%), Physiological Tremor(4.5%),Cerebellar/rubral Tremor(3.4%), Thyrotoxic tremor(3.4%), and Neuropathic tremor(3.4%),this was agreed with previous study by Garima Shukla[36].

The mean age of studied cases was 40.63 years with wide range between 14-76 years. Males outnumbered females in the study (59.1% and 40.9% respectively), The reasons for male preponderance in India are several; women in India usually ignore symptoms, especially those which do not hamper daily activities. this was very similar to as previously described by Findley L,T, Roller WC in 1987 [37] .

Few differences in the characteristics of tremor in patients with ET were observed, compared to published reports. Less than half (40%) of our patients reported lack of progression in their tremor and all had frequency of tremor in the higher range;

High-frequency tremor seen in our patients may be partially due to the fact that our patients were younger (mean age was 42.63 years). With advancing age usually the amplitude increases and frequency decreases, thus making the tremor more disabling.

The reason why most of our patients did not report progression may be that the average duration of the tremor in our series was only about 5 years, thus, they may not have experienced considerable; deterioration till the time they presented to us.

Mild asymmetry is known in ET, this was also seen in the present study. The anatomical distribution of tremor was also similar to that reported previously.

The characteristic involvement of the hands with head and voice tremor with relative sparing of legs helps in differentiating severe ET from Parkinsonian tremor. Alcohol responsiveness, considered diagnostic of ET, has been reported very commonly in patients of ET. This could not be assessed in our series as alcohol consumption was reported in only 12 patients, and 9 of these did not observe any

major change in the tremor with alcohol. A similar observation was reported by Louis et al."

Family history was positive in 46.5% of ET patients in the present study, very similar to the 62.5% positivity seen in the large population of ET patients observed by Louis et al. The autosomal dominant pattern was observed in only a few families, due; to known variable penetration, as also due to low certainty with which many patients give the family history.

About 42 ET patients were treated with Propranolol in the dose range of 60 to 180 mgs/day, tremor magnitude as measured by surface EMG was reduced by approximately 30%, Side effects occurred in 10% of patients and included lightheadedness, fatigue, impotence, and bradycardia.

About ten ET patients were treated with primidone using doses from 50 to 450 mg/day. The mean reduction in tremor magnitude by surface EMG was approximately 40%.

The term 'dystonic tremor' is unacceptable to some authorities on Movement Disordersas 'dystonia-associated tremor' and 'dystonic tremor' have often been grouped under the rubric of ET variants or simply as accompanying movement disorders. However the Consensus Statement of the Movement Disorder Society has classified 'dystonic tremor' as a separate entity.

Among the 73 patients of ET seen by Louis et al, in their community based study, no patients had associated dystonia. This is because the diagnostic criteria proposed earlier by these authors were used for the diagnosis of ET and most of the patients with tremor in the body part affected by dystonia would have been excluded.

Although the commonest type of dystonia seen in previous studies, with tremor, is cervical dystonia, we found hand tremor (including dystonic writer's cramp) to be the commonest in our group of dystonic tremors. This could be explained by the fact that we strictly followed the definition of dystonic tremor and excluded patients who had dystonia with tremor affecting other unaffected body parts.

Most patients visiting our hospital belong to the lower socio-economic strata and these patients may not spend money and time on visiting a specialty clinic for cervical dystonia with head tremor till it becomes severe or is associated with pain. They may not visit a doctor for cosmetic reasons alone. This is confirmed by the community study of Louis et al, in which most of the patients were unconcerned about their tremor, and did not consult a doctor.

The Task specific Tremors was present in six patients (4 writing tremors, one musician, one tailor) with poor response to pharmacotherapy.

Six patient’s had drug induced tremors (one beta receptor agonists, two sodium valproate, one lithium, one neuroleptics, and one tricyclic antidepressants).

Another 6 patients showed Enhanced physiologic tremor (three hyperthyroidism, three alcohol withdrawal) with moderate response to propronolol and benzodiazepines

We found a reasonable number of patients with psychogenic tremor; referral bias may again be an explanation for this occurrence, as we have a good Psychiatry department with exposure to movement disorders clinic.

Tremor was the commonest psychogenic movement disorder at about eight patients with psychogenic movement disorders among 200 consecutive patients with different movement disorders. Half of these 8 patients had psychogenic tremor with features of marked distractibility, change in tremor frequency, and entrainment of the tremor frequency to the tapping frequency.

The cerebellar type of tremor was present in three patients (one cerebellar infarct,one midbrain tumour and one post head injury) with poor response to pharmacotherapy.

Tremor Associated with Peripheral Neuropathy found in 3 patients (one HMSN, one AMSAN variant of gbs and CIDP) with moderate response to propronolol (40mg-120mgs).

Tremor rating scale is a simple clinical rating scale for clinical tremor analysis which can be used in OPD. The mean TRS score in our study was found to be 11.02 ±

5.36 with essential tremors presenting to us showed mean TRS of 11.45 ± 3.21 and similar observation was reported by Elan D. Louis, MD,[50]

When frequency analysis was done in our study using surface EMG essential tremor showed a mean frequency 9.69 ± 3.06 Hz which is in higher side of classical frequency range and this was agreed with study done by Elble RJ et al.[51]

Originally, it was proposed that ET has only synchronous activity (Growdon et al., 1975; Shahani and Young, 1976), whereas PD has only reciprocal alternating activity. Meanwhile, both forms of muscle activation have been found in either condition (Sabra and Hallett, 1984; Deuschl et al., 1987), and it has even become clear that in one and the same patient, both forms of muscle activity can occur (Elble, 1986).

Thus we can conclude that in our study ET has predominant 'fast frequency' type of tremor. This more over suggested the importance of surface EMG in differentiating such 'fast frequency' ET from enhanced physiologic tremor. Surface EMG pattern is classically synchronised in ET, where as a mixed pattern is seen in enhanced physiological tremor in comparison to previous study by (Calzetti et al.,1987)[53]

In concordance with American Academy of Neurology recommendation for use of surface EMG for kinesiologic analysis of movement disorder (Type C recommendation) (2000), surface EMG was done and electrophysiologic features were studied under three types of EMG burst patterns -

1) Synchronised pattern there is co-contraction burst of agonist and antagonist group of muscles.

2) Alternating pattern there is predominantly alternating activity of agonist and antagonist group of muscle.

3) A mixed pattern may look like a normal interference pattern without well defined bursting.

In our study 54.5% of patient showed synchronized SEMG pattern on analysis. Essential tremor was the commonest tremor among all tremors showing synchronized pattern and a statistically significant 76.9% ET showed classical synchronized pattern (p – 0.011). 23.07% ET patient had synchronized and mixed pattern, none showing alternate pattern.

However, alternate EMG burst pattern was shown by cerebellar tremor. The above burst patterns can be compared to Gronell, Alexandre et al (2004) study which showed SEMG has high diagnostic and predictive value that justifies its practice in movement disorder clinics.

The electrophysiologic features noted in these essential tremor patients were :

1) ET showed rhythmic burst of postural tremor on EMG.
2) Synchronised EMG burst pattern in 76.9% of clinically identified ET cases.
3) Tremor frequency greater than 4 Hz with frequency range of 6-16 Hz.
4) EMG showed a mean frequency of 9.69 ± 3.06 Hz.
5) Absence of rest tremors in ET or if present frequency 1.5 Hz lower than postural tremor
6) Absence of tremor latency from rest to postural position.

Comparable EMG recordings from these patients with 'neuropathic tremor' showed an intermediate situation. That was (1) the bursts of EMG activity were less well grouped than in the synchronous or alternating varieties of tremor and (2) they, at times, appeared to be synchronous in antagonistic muscles and, at other times, alternating.

EMG recordings from pairs of antagonistic muscle groups in the Physiological Tremor subjects were unremarkable and had the appearance of an 'interference pattern' ; in a few, discrete, synchronous bursts of EMG activity occurred.

In contrast with essential tremor, which was usually in one plane, the direction of the abnormal movement during the 'cerebellar tremor' was multi-planar and the large oscillations highly irregular and slow (2 to 4 Hz). Though the cerebellar tremors were usually absent with the limbs in repose, 'rubral tremors' were often present under those conditions though they increased considerably with activity and the above results were similar to study by Bhagwan T. Shahani et al (1976)[52].

The above electrophysiological features in our study are comparable with the criteria laid down by the MDS consensus statement. [19,23]

SUMMARY AND CONCLUSIONS

1. Eighty eight patients with non-parkinsonian tremors were studied with a sex distribution of male 59.1 per cent and females 40.9 per cent.

2. Age of the studied population was ranged from 14-76 with mean age of 42.63 years.

3. Essential Tremor was the most common non-parkinsonian tremor found in our study (59.1 per cent).

4. Dystonic tremor was being the second most common non-parkinsonian tremor found in our study.

5. Enhanced physiological, rubral, task specific, cerebellar, drug induced and alcohol withdrawal were the other types of non-parkinsonian tremors seen. All types of EMG burst activity was seen in such patients.

6. The mean TRS score was 11.02 ± 5.36 SD with a range of 3.5 – 24.

7. We observed that alcohol responsiveness could not be used as a diagnostic criterion for ET in India, as many patients are teetotalers.

8. The Rest tremor ET was associated with disease that was more severe, more disseminated (extending to other body regions), and of longer duration.

9. Positive family history was found in 24 out of the 52 (46.5 per cent) ET patients, it was definite in 4, probable in 15 and possible in 6 patients.

10. Three types of burst activity in EMG analysis were seen in our study namely synchronized, mixed and alternating pattern.

11. Classical synchronized EMG burst pattern was observed in 76.9 per cent ET patients (p-0.011) with mean frequency of 9.69 ± 3.06 Hz. Such ‘fast frequency’ ET can be differentiated from enhanced physiological tremor using synchronized surface EMG burst pattern.

ABBREVIATIONS AND ACRONYMS

- **TRS-Tremor Rating Scale**
- **ET-Essential Tremor**
- **RUB-Rubral Tremor**
- **PHY T-Physiological Tremor**
- **DRUD IND-Drug Induced Tremor**
- **ALCOL WT-Alcohol Withdrawal Tremor**
- **DYST T-DYSTONIC TREMOR**
- **TASK SP T-TASK SPECIFIC TREMOR**
- **CEREB T-CEREBELLAR TREMOR**
- **PSYC T-PSYCHOGENIC TREMOR**
- **NEUROP T-NEUROPATHIC TREMOR**
- **THYRO T-THYROTOXIC TREMOR**
- **SYN-SYNCHRONIZED**
- **HIGH FREG-HIGH FREGUENCY**

  V-Variable
- **DZ-DIAZEPAM**
- **ALTERN-ALTERNATING**
- **TFT-THYROID FUNCTION TEST**
- **NCS-NERVE CONDUCTION STUDY**
- **TREAT-TREATMENT**
- **ND-NOT DONE**
- **SMAN-SENSORY MOTOR AXONAL NEUROPATHY**
- **Y-YES**
- **No-no**
- **N-NORMAL**
- **AB-N-ABNORMAL**
- **PROPL-PROPRONOLOL**
- **PRIMD-PRIMIDONE**
- **CBZ-CARBAMAZEPINE**
- **SSRI-SELECTIVE SEROTONIN REUPTAKE INHIBITORS**
- **THP-TRIHEXYPHENIDYL**

ANNEXURE - 1

PROFORMA FOR EVLUATION OF TREMORS

1. Name
2. Age
3. Sex
4. Diagnosis
5. Tremor Rating Scale
6. Family History
7. PD Features
8. Drug History
9. Smoking History
10. Alcohol Intake
11. Investigation (Whichever Feasible)
    - (i) Hb%
    - (ii) RBS
    - (iii) FT3/TSH
    - (iv) RFT
    - (v) LFT
    - (vi) Serum Ammonia

(vii) NCS

(viii) CT Scan Brain / MRI

(ix) Peripheral Smear

(x) Others

ANNEXURE - 2

Tremor Research Group Rating Scale

1. Head Tremor : Subject is seated upright. The head is observed for 10 seconds in midposition and for 5 seconds each during several provocative maneuvers. First the subject is asked to rotate his or her head to the maximum lateral positions slowly in each direction. The subject is then asked to deviate his or her eyes to the maximum lateral position while the examiner touches the subject's chin gently.

0	=	No tremor
1	=	Tremor seen or felt during provocative maneuvers.
2	=	Mild tremor seen at midposition or moderate tremor seen with provactive maneuvers.
3	=	Moderate tremor seen at midposition or severe tremor seen with provactive maneuvers.
4	=	Severe tremor seen at midposition.

2a. Face Tremor : Subject is seated upright and asked to smile and pucker his or her lips, each 5 seconds. Tremor is specifically assessed for the lower facial muscles (excluding jaw and tongue) and upper face (eye closure).

0	=	No tremor
1	=	Mild tremor seen only with active muscle contraction.
2	=	Mild tremor seen at rest or moderate tremor seen with active muscle contraction.
3	=	Moderate tremor seen at rest or severe tremor seen with muscle contraction.
4	=	Severe tremor seen at rest.

2b. Tongue tremor : Subject is seated upright. The subject is asked to open his or her mouth for 5 seconds and then stick out his or her tongue 5 seconds.

0 = No tremor

1 = Mild tremor seen only with active muscle contraction.

2 = Mild tremor seen at rest or moderate tremor seen with active muscle contraction.

3 = Moderate tremor seen at rest or severe tremor seen with muscle contraction.

4 = Severe tremor seen at rest.

2c. Jaw Tremor : Subject is seated upright. The subject is asked to maximally open his or her mouth and clench the jaw for 5 seconds.

0 = No tremor

1 = Mild tremor seen only with active muscle contraction.

2 = Mild tremor seen at rest or moderate tremor seen with active muscle contraction.

3 = Moderate tremor seen at rest or severe tremor seen with muscle contraction.

4 = Severe tremor seen at rest.

3. Voice Tremor. First assess speech during normal conversation, then ask subject to produce an extended “aaa” sound and “eee” sound for 5 seconds each.

0 = No tremor

1 = Barely perceptible tremor only during provocative maneuver

2 = Mild but clear tremor present with speaking.

3 = Moderate tremor (no voice breaks)

4 = Severe tremor (with voice breaks or unintelligible speech).

4. Arm tremor : Subject is seated upright. Tremor is assessed during four arm maneuvers (rest, forward horizontal reach posture, lateral "wing" and kinesis) for 5 seconds in each posture. Left and right arms may be assessed simultaneously. Amplitude assessment should be estimated using the maximally displaced point of the hand at the point of greatest displacement along any single plane. For sample, the amplitude of a pure supination-pronation tremor, pivoting around the wrist, would be assessed either the thumb or fifth digit.

a) Rest Tremor : The subject should have his or her elbows on the arm rests. (If this is the previous assessment, no specific instructions should be given. If the subject did not naturally assume an acceptable arm position for elbows on the arm rests with hands resting freely.) Begin the second assessment only after the subject appears relaxed in the new position.

b) Forward outstretched postural tremor. Subject should bring his or her arms forward, slightly lateral to midline and parallel to the ground. The hand should be straight and the fingers slightly and comfortably abducted so that they do not touch each other.

c) Lateral wing beating postural tremor. Subject abducts his or her arms parallel to the ground and flexes the elbows so that the two hands do touch each other. The fingers are slightly and comfortably abducted so that they do not touch each other, with the pointer finger at shoulder height.

d) Kinetic tremor. Subjects extend only his or her pointer finger. The subject then touches a set object located at the same height (parallel to the ground) and slightly lateral to the midline. The subject then touches his or her own nose or chin and repeats this back-and-forth motion sometimes. Only the position along the trajectory

of greatest tremor amplitude is assessed. This will typically be either at the nose or chin or point of full extent.

e) Tremor while walking : Have the patient walk a minimum of 6m at a normal pace to and from the examiner and observe his or her hands Rest tremor.

0	=	No tremor
1	=	Tremor is barely visible or present only with mental provocation or reinforcement.
1.5	=	Tremor is visible, but is < 1cm amplitude.
2	=	Tremor is 1-3cm amplitude.
2.5	=	Tremor is 3-5cm amplitude
3	=	Tremor is 5-10cm amplitude
3.5	=	Tremor is 10-20cm amplitude
4	=	Tremor is > 20cm amplitude

Postural Tremor:

0	=	No tremor
1	=	Tremor is barely visible
1.5	=	Tremor is visible, but is < 1cm amplitude
2	=	Tremor is 1-3cm amplitude
2.5	=	Tremor is 3-5cm amplitude.
3	=	Tremor is 5-10cm amplitude
4	=	Tremor is > 20cm amplitude.

Kinetic tremor :

0	=	No tremor
1	=	Tremor is barely visible

1.5 = Tremor is visible, but is < 1cm amplitude

2 = Tremor is 1-3cm amplitude

2.5 = Tremor is 3-5cm amplitude.

3 = Tremor is 5-10cm amplitude

4 = Tremor is > 20cm amplitude.

Tremor while waling

0 = No tremor

1 = Tremor is barely visible

1.5 = Tremor is visible, but is < 1cm amplitude

2 = Tremor is 1-3cm amplitude

2.5 = Tremor is 3-5cm amplitude.

3 = Tremor is 5-10cm amplitude

4 = Tremor is > 20cm amplitude.

5. Trunk tremor: Subject is comfortably seated in a chair. The subject flexes both legs at the hips 30 degrees above parallel to the ground 5 seconds. The knees are passively bent so that the lower leg is perpendicular to the ground. The legs are not allowed to touch ground Tremor evaluated around the hip joints and the abdominal muscles.

0 = No tremor

1 = Tremor present only with hip flexion

2 = Obvious but mild tremor

3 = Moderate tremor

4 = Severe tremor

6. Leg tremor action : Subject is comfortably seated. The subject is asked to raise his or her legs parallel to the ground with knees extended 5 seconds. The legs are slightly abducted so that they do not touch. The tremor amplitude is assessed at the end of the feet.

0 = No tremor

1 = Barely perceptible tremor

2 = Obvious but mild tremor

3 = Moderate tremor; < 5cm amplitude at any point.

4 = Severe tremor; > 5cm amplitude.

7. Leg tremor rest : Subject is comfortably seated with knees flexed and feet resting on the ground. The tremor amplitude is assessed at of maximal displacement

0 = No tremor

1 = Barely perceptible tremor

2 = Obvious but mild tremor

3 = Moderate tremor; < 5cm amplitude at any point.

4 = Severe tremor; > 5cm amplitude.

8. Standing Tremor: Subject is standing, unaided if possible. The internal malleoli are 5cm apart. Arms are down at the sides. Tremor is observed at any point on the legs or trunk.

0 = No tremor

1 = Barely perceptile tremor

2 = Obvious but mile tremor

3 = Moderate tremor

4 = Severe tremor

9. Spiral Drawings : Ask the subject to draw the requested figures. Test each hand without leaving the hand or arm on the table. Use only a point pen.

0 = Normal

1 = Slightly tremulous. May cross lines occasionally.

2 = Moderately tremulous or crosses line frequently.

3 = Accomplishes the task with great difficulty. Figure still recognizable.

4 = Unable to complete drawing. Figure not recognizable.

10. Handwriting : Have patient write “Today is a nice day”

0 = Normal

1 = Mildly abnormal. Slightly untidy, tremulous.

2 = Moderately abnormal. Legible, but with considerable tremor.

3 = Markedly abnormal, illegible.

4 = Severely abnormal. Unable to keep pencil or pen on paper without holding with the other hand.

11. Hold pencil approximately 1mm above a point on a piece of paper for 10 seconds

0 = No tremor

1 = Tremor is barely visible

1.5 = Tremor is visible, but is < 1cm amplitude

2 = Tremor is 1-3cm amplitude

2.5 = Tremor is 3-5cm amplitude

3 = Tremor is 5-10cm amplitude

3.5 = Tremor is 10-20cm amplitude

4 = Tremor is > 20cm amplitude

12. Pour water from one glass into another, using Styrofoam coffee cups filled 1cm from top. Rated separately for right and left hands.

0 = Absolutely no visible tremor.

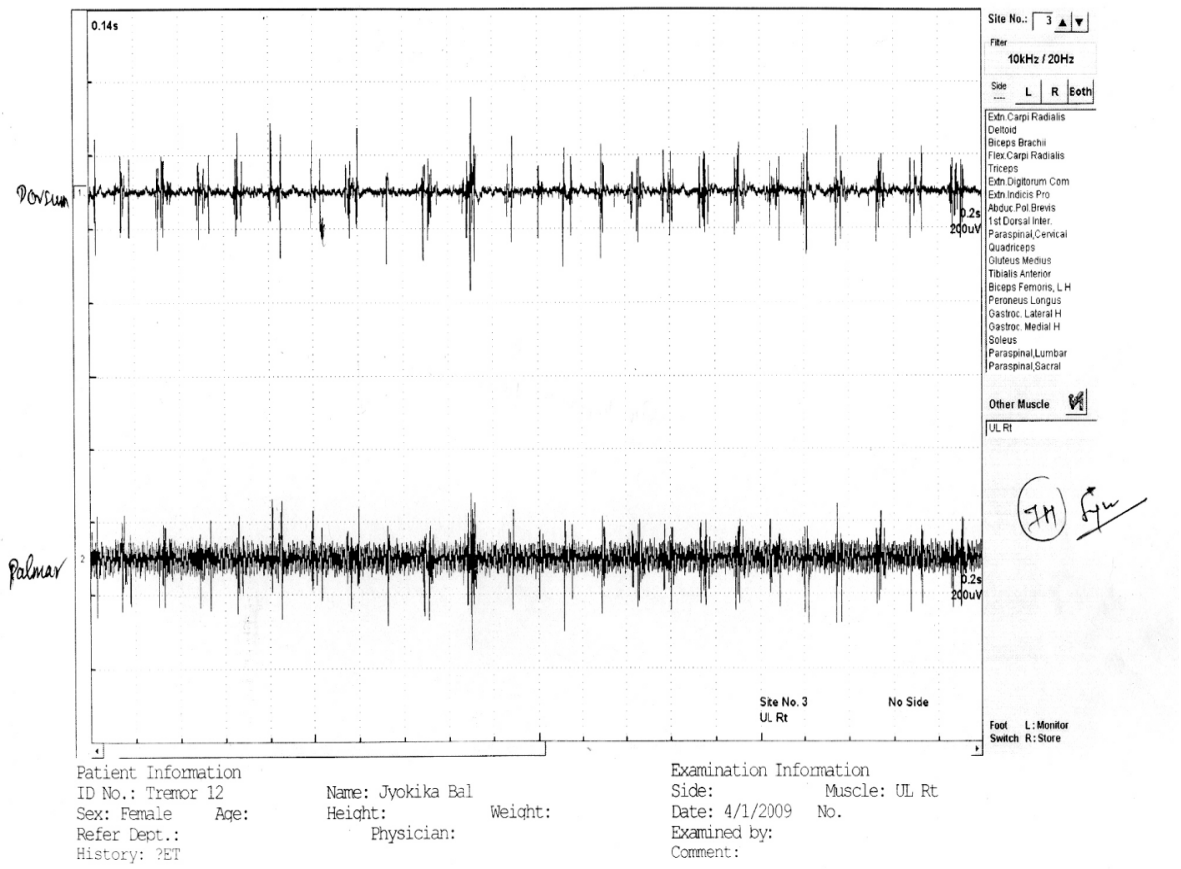
1 = More careful than a person without tremor, No water is spilled.

2 = Spills a small amount (< 10%)

3 = Spills large amount (10% -50%)

4 = Unable to pour without spilling most.

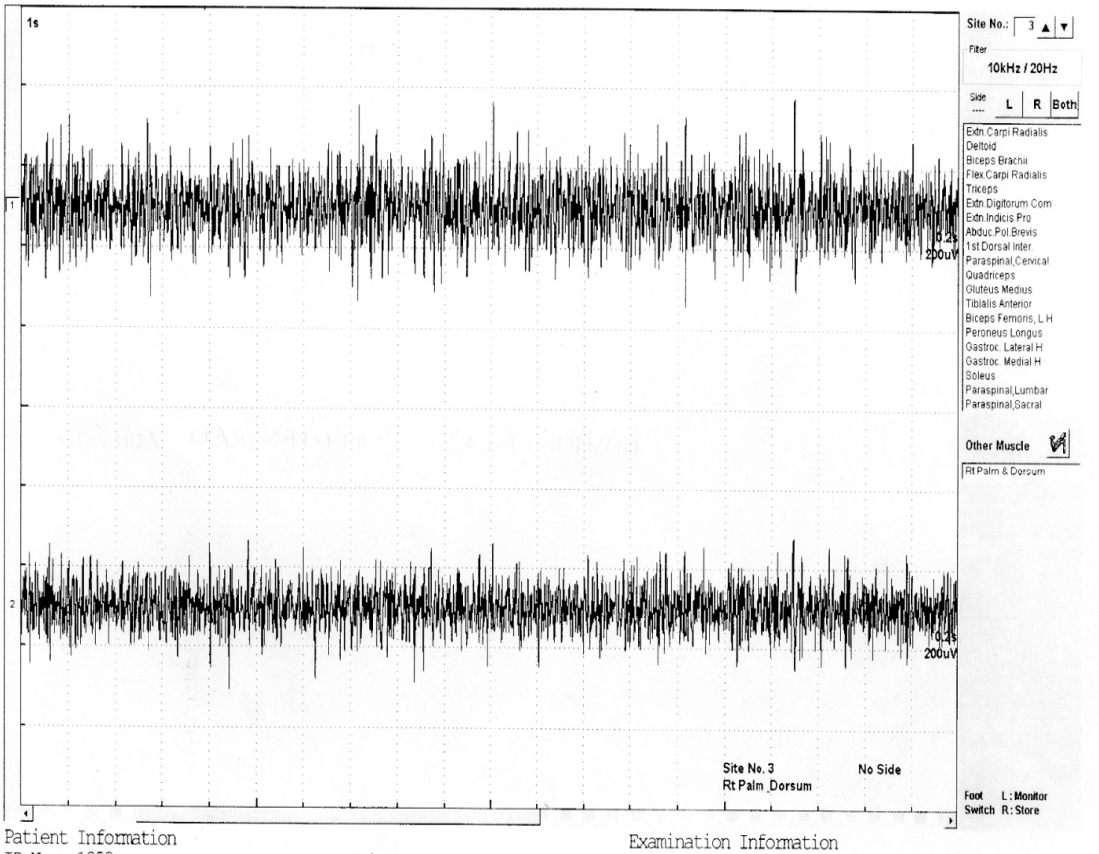
SYNCHRONISED BURST ACTIVITY



Patient Information
ID No.: Tremor 12 Name: Jyokika Bal
Sex: Female Age: Height: Weight:
Refer Dept.: Physician:
History: ?ET

Examination Information
Side: Muscle: UL Rt
Date: 4/1/2009 No.
Examined by:
Comment:

MIXED BURST ACTIVITY



Patient Information
ID No.: 1353 Name: Kondaiah
Sex: Male Age: 45 Height: 21161 Weight: 1395436
Refer Dept.: Gen.Med Physician: Dr.Manjunath
History: H/O:proximal weakness.Hypokalemia,Tremor rt leg

Examination Information
Side: Muscle: Rt Palm & Dorsum
Date: 7/28/2009 No.
Examined by:
Comment:

BIBLIOGRAPHY

1. Eindley L-J, Meeves L. Classification of Tremor. In: Disorders of' Movement: Clinical, Pharmacological and physiological aspects. Academic Press Ltd 1989.-505-19.

2. Movement disorder, Joseph Jankovic and Kathteen M Shannon, Chapter 75, p-2081 Vol-2, Neurology in Clinical Practice 5th Edn.

3. Electrophysiologic evaluation of movement disorders, Mark Hallett. Chapter 18, p-389. Electrodiagnosis in clinical Neurology. Michael J. Aminoff 5th Edn.

4. Clinical utility of surface EMG, SL Pullman; DS Goodin, MI Marquinez et al. Neurology, 2000; 55 : 171-177.

5. Handbook of essential tremors and other tremor disorder, Kelly E. Llyons, Rajesh Pahwa, 2005, p-10.

6. Louis ED. Essential Tremor. Arch Neurol 2000, 57(10) : 1522-24.

7. Gourie Devi M, Ramu MG, Venkataraman BS. Treatment of Parkinsonian's disease in "Ayurveda" (ancient Indian System of Medicine) : Discussion Paper JR Soc. Med 1991; 84 : 491-492.

8. Gaten DC. Tremore, Palpitatione, Convulsione et rigore In : Kuhn CG ed. Opera Omnia Krobloch. Germany : Lipsiae, 1824.

9. Parkinson J. Essay on the shaking Palsy London : Whittingham and Rouland for Sherwood, Neely and Jones, 1817.

10. Charcot JM. Lecons sur less Maladies du systeme Nerveux Faites a la Salpetriere, Delahaye et Le Cronsnier, 1880 : 155-188.

11. Dupuis MJM, Delvaide PJ, Bouequey D, Gonsette RE. Homolateral disappearance of essential tremor after cerebellar stroke. Mov. Disorder 1989; 4(2) : 183-187.

12. Hassler R. Zur. Pathologischen Anatomic des senilen und des parkinsonistischen tremor. J. Psychol Neurology (lp2) 1939, 44 : 193-230.

13. Mylle G, Van Bogaert L. DU tremblement essential non familial – Mschr Psychat Neurol. 1948; 115 : 80-90.

14. Rajput AH, Rozdilsky B, Ang L, Rajput A. Significance of Parkinsonian manifestations in essential tremor. Can J. Neurol Science 1993; 20: 114 – 117.

15. Stibler H, Kjeuin KG. Isoelectric focusing and electrophoresis of the CSF protein in tremor of different origins. J. Neurol Sci. 1976; 30 : 269-285.

16. Mally J, Baranyi M, Vizi ES. Change in the concentration of aminoacids in CSF and sorum of patients with essential tremor. J Neural Trans. 1996; 103 : 555-560.

17. Siegel GJ, Agranoff B, Albers RW, Fisher JK, Usler MD, eds. Basic neurochemistry : Molecular cellular and medical aspects. 6th Ed. New York. Lipincott – Raven 1999.

18. Pahwa R, Ryons K, Hubble J.P., Busenbark K, Rienerth JD, Pahwa AK. Double Blind controlled trial of gabupentive in essential tremor. Mor Disorder 1998, 13(3) : 465-467.

19. Deuschl G, Bain P. Brun M. Consensus statement of the movement Disorder Society on tremor. Ad. Hoc Scientific Committee. Mov. Disorder 1998; 13 (suppl 3) : 2-23.

20. Eible RJ, Higgins G, Leffler K, Hughes L. Factors influencing the amplitude and frequency of essential. Mov Disorder 1994; 9(6) : 589-596.

21. Elble RJ, Brilliant M, Lefflen K, Higginc C. Quantification of essential tremors in writing and drawing. Mov. Disord 1996; 11 : 70-78.

22. Deuschl G, Roethsen J, Lindermann M, Krack P. The pathophysiology of tremor. Muscle nerve 2001; 24 : 716-735.

23. Routine Neurophysiologic tremor analysis as a diagnostic tool for essential tremor. A prospective study. Gironell, Alexandre, Kalisevsky, Jaime et al. Dec 2004, vol 21 p 446-450.

24. Dr. Sybille Spicker, Verena Ströle, Alexandra Sailen et al, Validity of long term electromyography in the quantification of tremor. The movement Disorder Society, 1997.

25. Time frequency Analysis of tremors, O' Suilleabhain and J.Y Matsumoto, Brain, Vol 121 (1998) Issue 11, p-2127 – 2134.

26. Identification of physchogenic, dystonic and other organic tremors by a coherence entraintment trest. Mc Auley, J-Mov. Disorder, March 2004; 19(3) : 253-67.

27. Clinical and Surface EMG characteristics of valproate induced tremors, M. Mehindiratta, M. Satyawani, S. Gupta, Khwaja G.A., Electromyography and clinical neurophysiology 2005, vol 45, p-117-182.

28. Winker GF, Young RR. The control of essential tremor by Propranolol. Trans Am. Neurol Assoc 1971, 96 : 66-68.

29. Findley LJ, Calzetti S. Double blind controlled study of primidone in essential tremor : Preliminary results, Br. Med. J (Clin Res Ed) 1982, 285-608.

30. Connor GS. A randomized double-blind placebo controlled trial of topiramate treatment for essential tremor. Neurology 2002; 59 : 132-134.

31. Koller WC, Royse VL. Efficacy of primidone in essential tremor. Neurology 1986; 36 : 121-124.

32. Modugno N, Priori A, Berardelli A et al. Botulnium toxin restores presynaptic inhibition of group Ia afferents in patients with essential tremor. Muscle Nerve 1998; 21(12) : 1701-1705.

33. Lyons KE, Pahwa R, Comella CL et al. Benefits and risk of pharmacological treatment for essential tremor. Drug Saf 2003; 26 : 461-481.

34. Rehncrona S, Johnels B, Widner H, Tornqvist AL, Hariz M, Sydow O. Long term efficacy of thalamic deep brain stimulation for tremor: double-blind assessments. Mov Disorder 2003; 18(2) : 163-170.

35. Practice Parameter: Therapies for essential tremor T.A. Zesiewicz, MD; R. Elble, MD, PhD, NEUROLOGY 2005; 64: 2008–2020.

36. A clinical study of non-parkinsonian and non-cerebellar tremor at a specialty movement disorders clinic, Garima Shukla, Neurology India June 2004 Vol 52. Issue 2.

37. Psychogenic Tremor: Long Term Prognosis in Patients with Electrophysiologically-Confirmed Disease Andrew McKeon, MB, MRCPI,* J. Eric Ahlskog Movement Disorders Vol. 24, No. 1, 2009, pp. 72–76

38. Findley L, T, Roller WC. E s s e n t i a l Tremor: A review. Neurology 1987;37:119

39. Louis ED, Kord B, Wendt KJ, Cameron G. Clinical Characteristics of Essential Tremor: Data from a community-based study. Mov Disord 1998;13:803-8
40. Lou J S , Jankovic J. Essential tremor: Clinical correlates in 350 patients. Neurology1991;41:234-8.
41. Dubinsky RM, Gray CS, Roller WC. Essential tremor and dystonia. Neurology 1993;43:2382-4
42. Raut.akorpi I, Tdkala J. Marttila RJ, Sievers K, Rhine UK. Essential tremor in a Finnish population. Acta Neurol Seand 1982; 66:58-67.
43. Findley L I , Gresty MA. Tremor. Br J Hosp Med 1981; 26:16-32.
44. Jankovic J. Essential Tremor: Clinical characteristics .Neurology 2000;54:821
45. Rest Tremor in Patients With Essential Tremor *Oren Cohen,* MD; *Seh Pullman,* MD, *Arch Neurol. 2003;60:405-410*
46. Pharmacologic Treatment of Tremor *movement disorder* Vol. 13. Supplement 3, 1998. pp. 90-100
47. Nonparkinsonian Tremors Paul G. Wasielewski, MD *Clinical Neuropharmacology* Vol. 23, No. 5, pp. 233–238
48. TREATMENT OF TREMOR Continuum: Lifelong Learning Neurol 2007:13(1):58–71
49. A clinical study of non-parkinsonian and non-cerebellar tremor at a specialty movement disorders clinic, Garima Shukla, Neurology India June 2004 Vol 52 Issue 2

50. Elan D. Louis, MD et al., Comparison of Clinical vs. Electrophysiological Methods of Diagnosing of Essential Tremor , Movement Disorders Vol. 16, No. 4, 2001, pp. 668–673
51. Elble RJ, Higgins C, Leffler K, Hughes L. Factors influencing the amplitude and frequency of essential tremor. Mov Disord 1994;9: 589–596
52. Bhagwan T. Shahani et al Physiological and pharmacological aids in the differential diagnosis of tremor, Journal of Neurology, Neurosurgery, and Psychiatry, 1976, 39, 772-783.
53. Calzetti et al., Frequency/amplitude characteristics of postural tremor of the hands in a population of patients with bilateral essential tremor: implications for the classification and mechanism of essential tremor. Journal of Neurology, Neurosurgery, and Psychiatry 1987; 50:561-567